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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE Copy

In re application of:			
Yongwei CAO *et al.*		Art Unit:	1656
Appln. No.:	09/404,520	Examiner:	T.E. STRZELECKA
Filed:	September 23, 1999	Atty. Docket:	16517.081
For:	***Emericella nidulans* Genome Sequence and Uses Thereof**		

#16

Petition under 37 C.F.R. §1.144

Commissioner for Patents
Washington, DC 20231

Sir:

Responsive to the final Office Action mailed December 28, 2001, with a three (3) month shortened statutory period for response, Applicants hereby petition the Commissioner to review and require withdrawal of the requirement for restriction in the above-identified application and require consideration of the patentability of the full scope of the pending claims. This petition is timely-filed prior to the expiration of the three-month shortened statutory period for response and before appeal.

A. Statement of Facts

1. Application Serial No. 09/404,520 was filed September 9, 1999, and disclosed about 12,000 genes or partial genes of the filamentous fungus *Emericella nidulans*, also commonly known as *Aspergillus nidulans*. The DNA fragments from genomic sequencing were assembled into large contiguous sequences, resulting in 16,206 separate DNA sequences, disclosed as SEQ ID NOS: 1 – 16206. The sequences were analyzed by homology-based and predictive based methods to identify 11,958 predicted genes disclosed in the sequence list as SEQ ID NO: 16207 through SEQ ID NO: 28165. *See* Ser. No. 09/404,520 at 4, lines 10 to 23.

2. The application was originally filed with 46 claims. In the Office Action mailed February 12, 2001, the Examiner required restriction of the claims to one of eleven groups. *See* Office Action mailed February 12, 2001 at 2-4. In the same Office Action, the Examiner required Applicants to elect a single nucleic acid sequence for examination, citing MPEP §803.04. *Id.* at 9.

3. In response to the restriction requirement imposed by the Examiner, Applicants provisionally elected, with traverse, the subject matter of Group XI comprising original claims 29 and 30 and submitted a preliminary amendment which included characterizing the claimed subject matter by a Markush group including 11,698 genes and partial genes having nucleotide sequences selected from the group consisting of SEQ ID NO 16207 through 27905. *See* Response to Restriction Requirement and Preliminary Amendment at 2. Because these genes were identified by homology-based methods, they all have an assigned function.

Although Applicants expressed their belief that the claimed invention should be examined without the sequence restriction, applicants provisionally elected a 100 nucleotide sequence set (SEQ ID NOS: 16207 through 16306) and the single sequence (SEQ ID NO 16207) for examination. *See* Response to Restriction Requirement and Preliminary Amendment at 2. The then-amended claim 29 and newly added claims 57 and 58 illustrate the key aspects of the invention as follows:

> 29. (Amended) Computer readable medium having recorded thereon at least 100 of the nucleotide sequences selected from the group consisting of SEQ ID NO: 16207 through SEQ ID NO: 27905 and complements thereof.
>
> 57. (New) A computer based system comprising computer readable medium of claim 29, input means for receiving a target sequence, means for identifying fragments of sequence recorded in said computer readable medium which are homologous to a target sequence, and an output means for outputting identified homologous sequences.
>
> 58. (New) A method of identifying nucleotide sequence comprising comparing target sequence to a sequence stored in computer readable medium of claim 29.

Id. at 2-3. Finally, Applicants requested an interview with the Examiner based on Applicants' belief that the restriction to a single nucleotide sequence prevented the examination of the Applicants' claimed invention. *Id.* at 2.

4. In the Office Action mailed May 23, 2001, the Examiner indicated that claims 57 and 58 contained allowable subject matter, but repeated the election of a single nucleotide sequence requirement citing MPEP §803.04. *See* Office Action mailed May 23, 2001 at 2.

5. In the Amendment of October 23, 2001, Applicants canceled all pending claims except claims 57 and 58. Amendment dated October 23, 2001 at 1. Applicants then rewrote claims 57 and 58 in independent form[1]. *Id.* at 2.

6. On October 26, 2001, Examiner Strzelecka spoke with Applicants' attorney and stated that the application could be passed to issue if the claims were amended to refer only to the single sequence searched. Applicants refused to authorize an Examiner's amendment limiting the claims to a single sequence because a computer system and search method limited to a single sequence would be essentially valueless and merely a sham easily avoided by others who could use the full value of applicants' invention with impunity.

7. On December 28, 2001, a final Office Action was mailed leaving applicants with a Hobson's choice of limiting the otherwise allowable claims to a single sequence or abandoning the application. *See* Final Office Action at 2.

8. The United States Patent and Trademark Office (hereinafter, "USPTO") implemented a policy, published in 1192 O.G. 68 (November 19, 1996) of searching up to ten sequences. The USPTO officially adopted this policy in MPEP §803.04,[2] which permits a reasonable number of

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[1] The claims currently pending in the application read as follows:

57. A computer based system comprising computer readable medium having recorded therein at least 100 nucleotide sequences including sequences selected from the group consisting of SEQ ID NO: 16207 through SEQ ID NO: 27905 and complements thereof, input means for receiving a target sequence, means for identifying fragments of sequence recorded in said computer readable medium which are homologous to a target sequence, and an output means for outputting identified homologous sequences.

58. A method of identifying nucleotide sequence comprising comparing target sequence to a sequence stored in computer readable medium having recorded thereon at least 100 nucleotide sequences including sequences selected from the group consisting of SEQ ID NO: 16207 through SEQ ID NO: 27905 and complements thereof.

[2] MPEP § 803.04 reads in relevant part:

> Nucleotide sequences encoding different proteins are structurally distinct chemical compounds and are unrelated to one another. These sequences are thus deemed to normally constitute independent and distinct inventions within the meaning of 35 U.S.C. 121. Absent evidence to the contrary, each such nucleotide sequence is presumed to represent an independent and distinct invention, subject to a restriction requirement pursuant to 35 U.S.C. 121 and 37 CFR 1.141 *et seq.* Nevertheless, to further aid the biotechnology industry in protecting its intellectual property without creating an undue burden on the Office, the Commissioner has decided *sua sponte* to partially waive the requirements of 37 CFR 1.141 *et seq.* and permit a reasonable number of such

nucleotide sequences to be examined in a single application. The current, unofficial but de facto, policy now implemented by the USPTO, with respect to applications containing subject matter directed to nucleotide or amino acid sequences, is an outright refusal to examine more than a single sequence in any application.[3]

B. Summary of Arguments

Applicants respectfully petition the Commissioner to review the restriction and election requirement in the above-captioned matter. The required restriction and election of a single sequence are overly restrictive and do not follow the directives and standards published in the MPEP, which the USPTO and its employees are required to abide by *Patlex Corp. v. Mossinghoff*, 771 F.2d 480, 226 U.S.P.Q. 985, 989 (Fed. Cir. 1985) (citing *In re Kaghan*, 387 F.2d 398, 401, 156 U.S.P.Q. 130, 132, 55 C.C.P.A. 844 (1967)). ("The MPEP is primarily a set of instructions to the examining corps of the PTO from the Commissioner. It governs the details of the PTO examination, is made available to the public and describes procedures on which the public can rely.")

Moreover, both the de facto and the published policies effectively deny Applicants their statutory right to their invention which, in this case, is properly set forth in a claim comprising a Markush group of a plurality of sequences. The requirement that Applicants elect only a single nucleotide sequence for issuance in the present application effectively nullifies the advantages

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nucleotide sequences to be claimed in a single application. See *Examination of Patent Applications Containing Nucleotide Sequences,* 1192 O.G. 68 (November 19, 1996).

> It has been determined that normally ten sequences constitute a reasonable number for examination purposes. Accordingly, in most cases, up to ten independent and distinct nucleotide sequences will be examined in a single application without restriction. In addition to the specifically selected sequences, those sequences which are patentably indistinct from the selected sequences will also be examined. Furthermore, nucleotide sequences encoding the same protein are not considered to be independent and distinct inventions and will continue to be examined together.

[3] The USPTO altered this policy without soliciting any comment from the public or publishing its new policy.

and value of the disclosed invention. In the instant case, the single sequence policy effectively forces applicants to file 11,698 applications to obtain exclusive rights to their invention. If, for the sake of argument, the nominal out of pocket cost for a patent from cradle to grave including filing, issue and maintenance fees is $8,000, Applicants are faced with the unconscionable economic burden of about $100 million (about 1% of the annual USPTO budget). Moreover, even this expenditure would not allow Applicants to claim what they regard as their invention.

Applicants respectfully submit that the Commissioner has effectively denied Applicants their right to claim their invention.

C. The Requirement to Elect a Single Sequence to Issue in the Claims of the Present Case does not Comply with USPTO Published Rules and Practice and Denies Applicants Rights in the Subject Matter Which They Regard as Their Invention

(a) The USPTO policy does not comply with the rules and standards published in the MPEP

Applicants are claiming a proper Markush group under MPEP §2173.05(h) directed to a computer based system capable of identifying any one of the 100 sequences, or fragments thereof, stored within and a method of identifying the same. MPEP §803.04 directs the USPTO on the proper examination of such claims as those in the present application. That section reads in relevant part:

> Examples of typical nucleotide sequence claims impacted by the partial waiver of 37 CFR 1.141 *et seq*. (and the partial waiver of 37 CFR 1.475 and 1.499 *et seq*., see MPEP § 1850) include:
>
> (A) an isolated and purified DNA fragment comprising DNA having at least 95% identity to a DNA sequence selected from SEQ ID Nos. 1-1,000;
>
> (B) a combination of DNA fragments comprising SEQ ID Nos. 1-1,000; and
>
> (C) a combination of DNA fragments, said combination containing at least thirty different DNA fragments selected from SEQ ID Nos. 1-1,000.

> Applications claiming more than ten individual independent and distinct nucleotide sequences in alternative form, such as set forth in example (A), will be subject to a restriction requirement. Only the ten nucleotide sequences selected in response to the restriction requirement and any other claimed sequences which are patentably indistinct therefrom will be examined.
>
> Applications claiming only a combination of nucleotide sequences, such as set forth in example (B), will generally not be subject to a restriction requirement. The presence of one novel and nonobvious sequence within the combination will render the entire combination allowable. The combination will be searched until one nucleotide sequence is found to be allowable. The order of searching will be chosen by the examiner to maximize the identification of an allowable sequence. If no individual nucleotide sequence is found to be allowable, the examiner will consider whether the combination of sequences taken as a whole renders the claim allowable.
>
> Applications containing only composition claims reciting different combinations of individual nucleotide sequences, such as set forth in example (C), will be subject to a restriction requirement. Applicants will be required to select one combination for examination. If the selected combination contains ten or fewer sequences, all of the sequences of the combination will be searched. If the selected combination contains more than ten sequences, the combination will be examined following the procedures set forth above for example (B). More specifically, the combination will be searched until one nucleotide sequence is found to be allowable with the examiner choosing the order of search to maximize the identification of an allowable sequence. The identification of any allowable sequence(s) will cause all combinations containing the allowed sequence(s) to be allowed.

MPEP §803.04 (emphasis added). The present application includes claims of the type addressed in part (C) above. However, the USPTO refuses to comply with its own published directives in examining the claims of this case.

Although the MPEP is not law, it is a directive and requires compliance by USPTO employees. *See In re Int'l Flavors & Fragrances, Inc.* 183 F.3d 1361, 1366, 51 U.S.P.Q.2d 1513 (Fed. Cir. 1999) ("although [the MPEP] does not have the force of law, is well known to those registered to practice in the PTO and reflects the presumptions under which the PTO operates") *citing Critikon, Inc. v. Becton Dickins Vascular Access, Inc.,* 120 F.3d 1253, 1257, 43 U.S.P.Q.2d 1666, 1669 (Fed. Cir. 1997); *In re Portola Pkg., Inc.* 110 F.3d 786, 788, 42 U.S.P.Q.2d 1295, 1297 (Fed. Cir. 1997) ("[t]he MPEP does not have the force and effect of law; however, it is entitled to judicial notice as the agency's official interpretation of statutes and regulations, provided it is not in conflict with the statutes and regulations") *citing Refac Int'l, Ltd. v. Lotus Dev. Corp.,* 81 F.3d 1576, 1584 n.2, 38 U.S.P.Q.2d 1665, 1671 n.2 (Fed. Cir. 1996).

By forcing Applicants to select a single sequence to issue as the sole member of the Markush group of the claims, the PTO ignores its own internal practice and directives as required by the MPEP. Applicants are entitled under the published directives to examination of their Markush claims. As this has been determined to be the case, Applicants are at least entitled to the 100 sequences selected, if not entitled to the examination of the full scope of their claims.

(b) The application of the current policy of the USPTO effectively denies Applicants their statutory rights in the disclosed invention.

Applicants' claims are directed to a computer based system comprising a computer readable medium having recorded thereon at least 100 nucleotide sequences selected from the group consisting of SEQ ID NO: 16207 through SEQ ID NO: 27905 and complements thereof and methods for identifying a particular sequence within this group. By requiring Applicants to select only a single sequence to issue in the claims, the actions of the Examiner effectively redefined Applicants' invention.

Moreover, Applicants are not claiming nucleotide sequences in isolation. The claims are directed to a computer based system and a method which allows one to search the genome of the filamentous fungus *Emericella nidulans* for a target sequence, a fragment of that sequence, or a complement. Not only does implementing an election of a single sequence in the present application effectively destroy the value of the invention as a tool for locating specific sequences in the genome of this fungus, but it is also an attempt to rewrite the claims to another invention. In other words, the claims in the present application have been effectively rejected under 35 U.S.C. §121 because of the Examiner's belief that they are directed to "independent and distinct" inventions. Final Office Action at page 2. However, imposing this type of rejection for a Markush claim is improper as a matter of law. *In re Weber,* 580 F.2d 455, 459, 198 U.S.P.Q. 328, 332 (C.C.P.A. 1978) (holding "that a rejection [of a Markush claim] under §121 violates the basic right of the applicant to claim his invention as he chooses"). As stated above, the Applicants' invention is not directed to a single nucleotide or even a group of nucleotides, but rather to tools and methods for identifying a particular sequence or fragment thereof in the genome of *Emericella nidulans.* Therefore, the restriction requirement in the present application is improper.

Applicants' own experience supports these positions. For instance, based on Applicants' experience with multi-sequence queries to public sequence databases, e.g. ncbi, embl, swiss-prot, etc., Applicants believe that the added cost of multi-sequence searching is merely a small increment of the cost of a single sequence search. In light of this information, Applicants would gladly pay a real cost search fee. The benefits of higher search fees might not accrue to the USPTO. Applicants submit this is a political problem for the USPTO that merely serves as evidence that the current policy is arbitrary and capricious with no objective foundation to serving the constitutional rights of applicants.

As applicants have argued, there are several less restrictive, alternative solutions available to aid the USPTO in its efforts to fairly search and prosecute applications involving nucleotide and amino acid sequences. For example, the Commissioner could set up a contractor with access to the USPTO sequence data bases for at cost searching at an applicant's option. Another possible alternative would be for the Commissioner to petition Congress to amend the law to require publication of all applications with the associated sequence listings so that applicants themselves could perform novelty searches after 18 months from filing. These proposed solutions, as well as many others, do not deny an applicant the right to the full scope of the invention to which he is entitled.

D. Conclusion

In view of the arguments above, including the policies published in the MPEP and alternative methods available for operating the PTO to effect multiple sequence searching at a reasonable cost, applicants specifically petition the Commissioner to return this application to the Examiner with instructions to examine 100 of the selected sequences recited in claims 57 and 58.

Arnold & Porter check number **200948** submitted herewith, includes payment of the fee of $130.00 for filing a Petition to the Commissioner (37 C.F.R. § 1.17(h)). In the event that extensions of time under 37 C.F.R. § 1.136, other than those otherwise provided for in the papers accompanying this Notice are required to prevent abandonment of this patent application, then such extensions of time are hereby petitioned.

The U.S. Patent and Trademark Office is hereby authorized to charge any fee deficiency, and/or credit any overpayment, to our Deposit Account No. 50-1824, referencing docket number 16517.081.

Respectfully submitted,

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